

10038574 052002
JCS RECEIVED PCTO 14 JAN 2002

FORM PTO-1390	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	ATTORNEY'S DOCKET NUMBER: 1501-1007
INTERNATIONAL APPLICATION NO.: PCT/SE00/01495		U.S. PPLN NO. (If known, see 37 CFR 1.5) 10/030924
INTERNATIONAL FILING DATE: 14 JULY 2000 (14.07.00)		PRIORITY DATE CLAIMED: 14 JULY 1999 (14.07.99)
TITLE OF INVENTION: MICRODIALYSIS PROBE		
APPLICANT(S) FOR DO/EO/US: Roger JOHANSSON		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.		
1.	<input checked="" type="checkbox"/>	This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2.	<input type="checkbox"/>	This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3.	<input checked="" type="checkbox"/>	This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4.	<input checked="" type="checkbox"/>	A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5.	<input checked="" type="checkbox"/>	A copy of the International Application as filed (35 U.S.C. 371(c)(2))
	a. <input checked="" type="checkbox"/>	is transmitted herewith (required only if not transmitted by the International Bureau).
	b. <input type="checkbox"/>	has been transmitted by the International Bureau. (see attached copy of PCT/IB/308)
	c. <input type="checkbox"/>	is not required, as the application was filed in the United States Receiving Office (RO/US).
6.	<input type="checkbox"/>	A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7.	<input type="checkbox"/>	Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
	a. <input type="checkbox"/>	are transmitted herewith (required only if not transmitted by the International Bureau).
	b. <input type="checkbox"/>	have been transmitted by the International Bureau.
	c. <input type="checkbox"/>	have not been made; however, the time limit for making such amendments has NOT expired.
	d. <input type="checkbox"/>	have not been made and will not be made.
8.	<input type="checkbox"/>	A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9.	<input type="checkbox"/>	An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10.	<input type="checkbox"/>	A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).
Item 11. to 16. below concern document(s) or information included:		
11.	<input checked="" type="checkbox"/>	An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12.	<input type="checkbox"/>	An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13.	<input checked="" type="checkbox"/>	A FIRST preliminary amendment.
	<input type="checkbox"/>	A SECOND or SUBSEQUENT preliminary amendment.
14.	<input type="checkbox"/>	A substitute specification.
15.	<input type="checkbox"/>	A change of power of attorney and/or address letter.
16.	<input checked="" type="checkbox"/>	Other items or information: INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT/IPEA/409), INTERNATIONAL SEARCH REPORT (PCT/ISA/210), APPLICATION DATA SHEET, ABSTRACT

1013 Filed PCT/PTO 14 JAN 2002

U.S. APPLICATION NO. (if known, see 37 CFR 1.1) 10/030924		INTERNATIONAL APPLICATION NO PCT/SE00/01495		ATTORNEY'S DOCKET NO 1501-1007	
17. <input checked="" type="checkbox"/> The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): Neither international preliminary examination fee (37 CFR1.482) nor international search fee (37 CFR1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$ 1,040.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$ 890.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$ 740.00 International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$ 710.00 International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$ 100.00 ENTER APPROPRIATE BASIC FEE AMOUNT = \$ 1040.00 Surcharge of \$130.00 for furnishing the oath or declaration later than 30 months from the earliest claimed priority date (37 CFR 1.492(e)). \$ 130.00				CALCULATIONS PTO USE ONLY	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$	
Total claims	8 - 20 =	0	X \$18.00	\$	
Independent claims	1 - 3 =	0	X \$84.00	\$	
MULTIPLE DEPENDENT CLAIMS(S) (if applicable)			+ \$280.00	\$	
TOTAL OF ABOVE CALCULATIONS =				\$ 1170.00	
Reduction of 1/2 for filing by small entity, if applicable. Applicant claims Small Entity Status under 37 CFR 1.27.				+	
SUBTOTAL =				\$ 1170.00	
Processing fee of \$130 for furnishing the English translation later than months from the earliest claimed priority date (37 CFR1.492(f)).				\$	
TOTAL NATIONAL FEE =				\$ 1170.00	
Fee for recording the enclosed assignment (37 CFR1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property				+	
TOTAL FEES ENCLOSED =				\$ 1170.00	
				Amount to be refunded:	
				charged:	
a.	<input checked="" type="checkbox"/>	A check in the amount of \$ 1170.00 to cover the above fees is enclosed.			
b.	<input type="checkbox"/>	Please charge my Deposit Account No. 25-0120 in the amount of \$ to cover the above fees. A duplicate copy of this sheet is enclosed.			
c.	<input checked="" type="checkbox"/>	The Commissioner is hereby authorized to charge any additional fees which may be required by 37 CFR 1.16 and 1.17, or credit any overpayment to Deposit Account No. 25-0120 . A duplicate copy of this sheet is enclosed.			
SEND ALL CORRESPONDENCE TO.					
YOUNG & THOMPSON 745 South 23rd Street 2nd Floor Arlington, VA 22202 (703) 521-2297 facsimile (703) 685-0573 Customer Number: 000466		January 14, 2002		By <u>Benoit Castel</u> Benoit Castel Attorney for Applicant Registration No. 35,041	

10/030924

JC13 Rec'd PCT/PTO 14 JAN 2002

PATENT
1501-1007

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of: Roger JOHANSSON

Appl. No.:

Group:

Filed:

January 14, 2002

Examiner:

For:

MICRODIALYSIS PROBE

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, DC 20231

January 14, 2002

Sir:

The following preliminary amendments and remarks are respectfully submitted in connection with the above-identified application.

Prior to the first Official Action and calculation of the filing fee, please substitute Claims 1-8 as originally filed, which appear on pages 8-9, with new Claims 1-8 as filed in the Article 34 amendment of September 4, 2001. The pages containing Claims 1-8 are marked "AMENDED SHEET" and are attached hereto.

IN THE ABSTRACT OF THE DISCLOSURE:

Please delete the Abstract of the Disclosure as originally filed which appears on the cover sheet of the Published Application. Add the Abstract of the Disclosure attached on a separate sheet attached hereto.

IN THE CLAIMS:

Please amend the claims as follows:

--5.(Amended) A microdialysis probe according to claim 1 characterized in that the distal end of the first tube (116) being sealed by means of a glue which holds and seals a plug (130) which comprises the position indicating object 130,410).

6.(Amended) A microdialysis probe according to claim 1, characterized in that said position indicating object is a plug made of any bio-compatible metal, alloy or amorphous compound which imparts the x-ray opaqueness necessary.

7.(Amended) A microdialysis probe according to claim 1, characterized in that said position indicating object is a plug made of compound dispersed in a glue sealing the probe which imparts the x-ray opaqueness to the plug.

8.(Amended) A microdialysis probe according to claim 1, characterized in that said position indicating object is a hollow object filled with air or the like.--

REMARKS

Claims 1-8 are pending in the present application.

Entry of the above amendments is earnestly solicited.
An early and favorable first action on the merits is earnestly requested.

Docket No. 1501-1007

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



Benoit Castel, Reg. No. 35,041

745 South 23rd Street
Arlington, VA 22202
Telephone (703) 521-2297

BC/bam
Attachments

VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE CLAIMS:

The claims have been amended as follows:

5. (Amended) A microdialysis probe according to any ~~of the preceding claims~~ claim 1 characterized in that the distal end of the first tube (116) being sealed by means of a glue which holds and seals a plug (130) which comprises the position indicating object (130,410).

6. (Amended) A microdialysis probe according to claim 1, ~~2 or 4,~~ characterized in that said position indicating object is a plug made of any bio-compatible metal, alloy or amorphous compound which imparts the x-ray opaqueness necessary.

7. (Amended) A microdialysis probe according to claim 1, ~~2 or 4,~~ characterized in that said position indicating object is a plug made of compound dispersed in a glue sealing the probe which imparts the x-ray opaqueness to the plug.

8. (Amended) A microdialysis probe according to claim 1 ~~or 3,~~ characterized in that said position indicating object is a hollow object filled with air or the like.

Claims

1. A microdialysis probe, comprising a dialysis membrane (115) located and supported between a closed distal end of the probe and a proximal end of the same, said membrane (115) essentially surrounding a first tube (116), said first tube and said membrane being so arranged, that a space (118) for passage of perfusion liquid is formed therebetween; said first tube exhibiting at least one through-hole for the passage of the perfusion liquid near the distal end of the first tube, said probe having inlet and outlet means (107,108) for perfusion liquid, **characterized** by the distal end of the space (118) being sealed in the presence of a position indicating object (130,410) imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.
2. A microdialysis probe according to claim 1, **characterized** in said position indicating object being an x-ray opaqueness giving object.
3. A microdialysis probe according to claim 1, **characterized** in said position indicating object being an object made from gold.
4. A microdialysis probe according to claim 1, **characterized** in said position indicating object being an object visible when using NMR (Nuclear Magnetic Resonance).
5. A microdialysis probe according to any of the preceding claims **characterized** in that the distal end of the first tube (116) being sealed by means of a glue which holds and seals a plug (130) which comprises the position indicating object (130,410).

6. A microdialysis probe according to claim 1, 2 or 4, **characterized** in that said position indicating object is a plug made of any bio-compatible metal, alloy or amorphous compound which imparts the x-ray opaqueness necessary.
- 5 7. A microdialysis probe according to claim 1, 2 or 4, **characterized** in that said position indicating object is a plug made of compound dispersed in the glue sealing the probe which imparts the x-ray opaqueness to the plug.
8. A microdialysis probe according to claim 1 or 3, **characterized** in that said
10 position indicating object is a hollow object filled with air or the like.

WO 01/03752

PCT/SE00/01495

ABSTRACT OF THE DISCLOSURE

A microdialysis probe includes a dialysis membrane (115,415) located and supported between a closed distal end of the probe and a proximal end of the same, the membrane (115,415) essentially surrounding a space (118,418) for passage of perfusion liquid. The probe has an inlet and outlet (107,108; 407,408) for perfusion liquid, characterized by presence of a position indicating object imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.

PTO/PCT Rec'd 09 MAY 2002

PATENT
1501-1007

IN THE U.S. PATENT AND TRADEMARK OFFICE

In re application of: Roger JOHANSSON

Appl. No.:

Group:

Filed:

January 14, 2002

Examiner:

For:

MICRODIALYSIS PROBE

PRELIMINARY AMENDMENTAssistant Commissioner for Patents
Washington, DC 20231

January 14, 2002

Sir:

The following preliminary amendments and remarks are respectfully submitted in connection with the above-identified application.

Prior to the first Official Action and calculation of the filing fee, please substitute Claims 1-8 as originally filed, which appear on pages 8-9, with new Claims 1-8 as filed in the Article 34 amendment of September 4, 2001. The pages containing Claims 1-8 are marked "AMENDED SHEET" and are attached hereto.

IN THE ABSTRACT OF THE DISCLOSURE:

Please delete the Abstract of the Disclosure as originally filed which appears on the cover sheet of the Published Application. Add the Abstract of the Disclosure attached on a separate sheet attached hereto.

IN THE CLAIMS:

Please amend the claims as follows:

--5.(Amended) A microdialysis probe according to claim 1 characterized in that the distal end of the first tube (116) being sealed by means of a glue which holds and seals a plug (130) which comprises the position indicating object 130,410).

6.(Amended) A microdialysis probe according to claim 1, characterized in that said position indicating object is a plug made of any bio-compatible metal, alloy or amorphous compound which imparts the x-ray opaqueness necessary.

7.(Amended) A microdialysis probe according to claim 1, characterized in that said position indicating object is a plug made of compound dispersed in a glue sealing the probe which imparts the x-ray opaqueness to the plug.

8.(Amended) A microdialysis probe according to claim 1, characterized in that said position indicating object is a hollow object filled with air or the like.--

REMARKS

Claims 1-8 are pending in the present application.

Entry of the above amendments is earnestly solicited.
An early and favorable first action on the merits is earnestly requested.

Docket No. 1501-1007

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

Benoit Castel, Reg. No. 35,041

745 South 23rd Street
Arlington, VA 22202
Telephone (703) 521-2297

BC/bam
Attachments

VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE CLAIMS:

The claims have been amended as follows:

5. (Amended) A microdialysis probe according to ~~any of~~
~~the preceding claims~~ claim 1 characterized in that the distal
end of the first tube (116) being sealed by means of a glue
which holds and seals a plug (130) which comprises the
position indicating object (130,410).

6. (Amended) A microdialysis probe according to claim 1, ~~2~~
~~or 4~~, characterized in that said position indicating object is
a plug made of any bio-compatible metal, alloy or amorphous
compound which imparts the x-ray opaqueness necessary.

7. (Amended) A microdialysis probe according to claim 1, ~~2~~
~~or 4~~, characterized in that said position indicating object is
a plug made of compound dispersed in a glue sealing the probe
which imparts the x-ray opaqueness to the plug.

8. (Amended) A microdialysis probe according to claim 1
~~or 2~~, characterized in that said position indicating object is
a hollow object filled with air or the like.

Claims

1. A microdialysis probe, comprising a dialysis membrane (115) located and supported between a closed distal end of the probe and a proximal end of the same, said membrane (115) essentially surrounding a first tube (116), said first tube and said membrane being so arranged, that a space (118) for passage of perfusion liquid is formed therebetween; said first tube exhibiting at least one through-hole for the passage of the perfusion liquid near the distal end of the first tube, said probe having inlet and outlet means (107,108) for perfusion liquid, **characterized** by the distal end of the space (118) being sealed in the presence of a position indicating object (130,410) imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.
2. A microdialysis probe according to claim 1, **characterized** in said position indicating object being an x-ray opaqueness giving object.
3. A microdialysis probe according to claim 1, **characterized** in said position indicating object being an object made from gold.
4. A microdialysis probe according to claim 1, **characterized** in said position indicating object being an object visible when using NMR (Nuclear Magnetic Resonance).
5. A microdialysis probe according to any of the preceding claims **characterized** in that the distal end of the first tube (116) being sealed by means of a glue which holds and seals a plug (130) which comprises the position indicating object (130,410).

6. A microdialysis probe according to claim 1, 2 or 4, **characterized** in that said position indicating object is a plug made of any bio-compatible metal, alloy or amorphous compound which imparts the x-ray opaqueness necessary.
- 5 7. A microdialysis probe according to claim 1, 2 or 4, **characterized** in that said position indicating object is a plug made of compound dispersed in the glue sealing the probe which imparts the x-ray opaqueness to the plug.
8. A microdialysis probe according to claim 1 or 3, **characterized** in that said
10 position indicating object is a hollow object filled with air or the like.

WO 01/03752

PCT/SE00/01495

ABSTRACT OF THE DISCLOSURE

A microdialysis probe includes a dialysis membrane (115,415) located and supported between a closed distal end of the probe and a proximal end of the same, the membrane (115,415) essentially surrounding a space (118,418) for passage of perfusion liquid. The probe has an inlet and outlet (107,108; 407,408) for perfusion liquid, characterized by presence of a position indicating object imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.

Microdialysis probe.

FIELD OF THE INVENTION

The invention relates to a microdialysis probe. Microdialysis probes of this kind are described in SE-C-434 214, US,A,5,735,832 and US,A,5,741,284.

The meaning of specific wordings in this text should be interpreted as follows:

The word probe should be interpreted also as catheter.

The inlet and outlet of the probe as described may in case of a reversed flow be used as outlet and inlet, respectively.

Perfusion liquid is the liquid used in the microdialysis, which is allowed to enter the probe and there take up substances from the surrounding tissue through a membrane.

The perfusion liquid becomes the dialysate after the dialysis.

Non-invasive investigating examination in this document refers to e.g. X-ray, NMR or the like techniques.

BACKGROUND OF THE INVENTION

Microdialysis is a method of examination in which a probe is inserted into tissue in vivo, such that one side of a semi-permeable membrane is in contact with tissue and extra cellular liquid and the other side is flushed or rinsed with a dialysis liquid (perfusate) which takes-up substances from the extra cellular liquid through the membrane. These substances can then be analyzed in the dialysate on or after exiting the probe.

Microdialysis probes are by nature fragile and very small, which requires great care in inserting and withdrawing the probe from the tissue in which it is used. However, it is also of great importance that the probe when inserted into tissue of a living person, is placed in the intended location such that when measuring the probe actually through microdialysis measures the intended chemical/biological variables that at each measurement is of interest. It is of course important in these measurements to know exactly what is measured.

The use of microdialysis becoming more frequent and common raises other problems such as monitoring and control of the probe during insertion and use. It is a fact that microdialysis provides a unique possibility to examine the equilibria of substances and/or the amounts present or missing of substances or to monitor specific changes in the status of substances connected with e.g. the use of medicaments, in surgery etc.

The monitoring and control of the probe position during insertion/withdrawal and use has been an obstacle in so far that the smallness and the material of the probe does not make possible the use of common methods for detecting the probe once the insertion has been started. This becomes more problematic the deeper into the tissue the microdialysis is to take place.

SUMMARY OF THE INVENTION.

It is thus an object of the invention is to provide a microdialysis probe, the location of which may be monitored and controlled using means such as X-rays or the like during insertion/withdrawal or during dialysis in order to facilitate the placement of the probe at a predetermined location and to control the location of the probe.

It is also an object of the invention to provide a microdialysis probe, which is suitable for the general use in living tissue when taking samples for e.g. diagnostic purposes.

In accordance with the invention, these and other objects evident from the description of the invention are accomplished in a microdialysis probe in that characterized by presence of a position indicating object imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.

BRIEF DESCRIPTION OF THE DRAWINGS.

The invention will now be described by way of example and with reference to the accompanying drawings in which:

5 Fig. 1 shows, partially in section, a first embodiment of a microdialysis probe in section according to the invention.

Fig. 2 shows a detailed view of the foremost part of the probe according to the embodiment as shown in Fig. 1.

10

Fig. 3 a - c shows in detail the sealing of the most distal part of the first tube according to the embodiment shown in Fig. 1 and Fig.2.

15

Fig. 4 shows a second embodiment of a microdialysis probe in section according to the invention.

DETAILED DESCRIPTION OF PREFERRED FORMS OF THE INVENTION.

20

A first embodiment of the microdialysis probe according to the invention is shown in Fig. 1 and Fig 2. The probe exhibits a distal end piece 110 comprised of glue which holds and seals a plug 130 within the distal part of a membrane 115. This comprises the foremost tip of the probe. The membrane 115 is preferably tubular. A proximal tubular fitting 111 and a proximal end piece 113 comprises the other end of the probe as such. The proximal tubular fitting 111 is permanently fastened to a proximal end piece 113. The proximal end of the membrane 115 is fastened to the proximal tubular fitting 111.

25

30

In the proximal end piece 113 two tubes 107 and 108 constituting the inlet to the probe and the outlet from the probe are connected to the probe, such as to let the perfusion liquid pass through the same. Note in the definitions above the possibility of reversed flow.

Within the membrane 115, which is in the form of a tube made from semi-permeable material, and also within the proximal tubular fitting 111, a first tube 116 extends essentially from the proximal end of the probe to the distal end. The first tube 116 is closed at the most distal end by a position indicating object, a plug 130, and exhibits at least one aperture 117 at or near the distal end. The aperture 117 constitutes a passage for the perfusion liquid entering the space 118 defined by the first tube 116 and the dialysis membrane 115 in combination with the proximal tubular fitting 111 and the distal tubular fitting 112. For the withdrawal of the perfusion liquid a second tube 119 extends from the proximal end of the probe and opens up into the same space 118 somewhere near to the proximal end of the probe thereby forming an exit for the perfusion liquid. The perfusion liquid has now become a dialysate having acquired substances exchanged over the semi-permeable membrane. The distal end piece 110 of the probe may e.g. be fastened in a permanent way to the distal end of the first tube 116.

To give a proper understanding of the invention, exemplary dimensions are given here. The length of the probe may be e.g. 5 cm from the most distal end of the same to the proximal part of the proximal tubular fitting 111. The length of the tubular fitting may be approximately 2 cm, thus the length of the membrane may be approximately 3 cm. The diameter of the proximal tubular fitting may be approximately 1 mm and the outer diameter of the membrane may be approximately 0.6 mm.

The plug 130 shown in Fig. 2 may preferably be manufactured from gold. Other materials may of course be used but the reason for using gold is the ductility and the relative opaqueness for X-rays and also the chemical and physiological inertness exhibited by gold.

In a second embodiment the plug 130 may be made such as to make the distal end of the microdialysis probe visible during examination using NMR (Nuclear Magnetic Resonance).

This plug could e.g. have the form of a hollow amorphous plug filled with air or the like, which would impart characteristics to the plug such that it will be possible to locate the plug using NMR.

One way of accomplishing the sealing at the distal end of the first tube 316 is shown in Fig 3 a - c.

In Fig. 3a) the form of an exemplary first tube 316 according to the invention is shown. The tube has been subjected to corbelling in order to widen the diameter of the same enough to accommodate the sealing plug 330.

In Fig. 3 b) a preferred embodiment of the sealing plug 330 is shown and in Fig. 3c) the first tube 316 with the sealing plug 330 in place is shown.

A second embodiment of the microdialysis probe according to the invention is shown in Fig. 4. The probe exhibits a distal end piece 410 and a distal tubular fitting 412. The distal tubular fitting 412 in combination with the end piece 410 comprises the foremost tip of the probe. A proximal tubular fitting 411 and a proximal end piece 413 comprises the other end of the probe as such. The proximal tubular fitting 411 is permanently fastened to a proximal end piece 413. A membrane 415 is fastened to the distal tubular fitting 412, the membrane 415 having a smaller diameter than the fitting. The membrane is preferably tubular. The fitting itself being closed at the most distal end thereof e.g. by using glue or the like, forming the distal end 410. The other end of the membrane 415 is fastened to the proximal tubular fitting 411.

In order to accomplish an X-ray opaqueness of the foremost part of the probe the distal end may be formed as a half-sphere or the like from a material which is opaque to X-rays or the X-ray opaqueness creating material may be incorporated in the glue as such.

In the end proximal piece 413 two tubes 407 and 408 constituting the inlet to the probe and the outlet from the probe are connected to the probe, such as to let the perfusion liquid pass through the same. Note above the possibility of reversed flow.

5

In this embodiment the dimensions of the probe will be approximately the same as in the embodiment described in connection with Fig 1.

Within the membrane 415, which is in the form of a tube made from semi-

10 permeable material, first tube 416 extends essentially from the proximal end of the probe to the distal end. The first tube 416 has a closed distal end and has at least one aperture 417 at or near the distal end. The aperture 417 constitutes a passage for the perfusion liquid entering the space 418 defined by the first tube 416 and the dialysis membrane 415 in combination with the proximal tubular fitting 411 and the distal
15 tubular fitting 412. For the withdrawal of the perfusion liquid a second tube 419 extends from the proximal end of the probe and opens up into the same space 418 somewhere near to the to the proximal end of the probe thereby forming an exit for the perfusion liquid.

20 In the same manner as has been described in connection with the first embodiment of the invention the end piece 410 sealing distal end of the probe may be made such as to make the same visible during examination using NMR (Nuclear Magnetic Resonance). This could e.g. be done by incorporating in the sealing glue a hollow amorphous plug filled with air or the like, which would impart characteristics to the
25 distal end of the probe such that it will be possible to locate the probe end by using NMR.

The invention has been described under reference to embodiments of the same. It should be understood that the above describes an exemplary embodiment of the
30 distal end of the probe itself and the constructive details thereof may vary within the scope of the claims or be independent of the constructive details of the distal end of

the probe depending on different embodiments of the invention. The scope of the invention however is described by the appended claims.

Claims

1. A microdialysis probe, comprising a dialysis membrane (115,215) located and supported between a closed distal end of the probe and a proximal end of the same, said membrane (115,215) essentially surrounding a space (118,218) for passage of perfusion liquid; said probe having inlet and outlet means (107,108; 207,208) for perfusion liquid, characterized by presence of a position indicating object (130,410) imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.
2. A microdialysis probe according to claim 1, characterized in said position indicating object being an x-ray opaqueness giving object.
3. A microdialysis probe according to claim 1, characterized in said position indicating object being an object visible when using NMR (Nuclear Magnetic Resonance).
4. A microdialysis probe according to any preceding claim, characterized in a first tube for inlet of perfusion liquid into the space between the membrane and the first tube, said first tube exhibiting a through-hole for the passage of the perfusion liquid near the distal end of the first tube, said most distal end of the first tube being sealed by a plug of said position indicating object.
5. A microdialysis probe according to claim 1, 2 or 4, characterized in that said position indicating object is a plug made of gold.
6. A microdialysis probe according to claim 1, 2 or 4, characterized in that said position indicating object is a plug made of any bio-compatible metal, alloy or amorphous compound which imparts the x-ray opaqueness necessary.

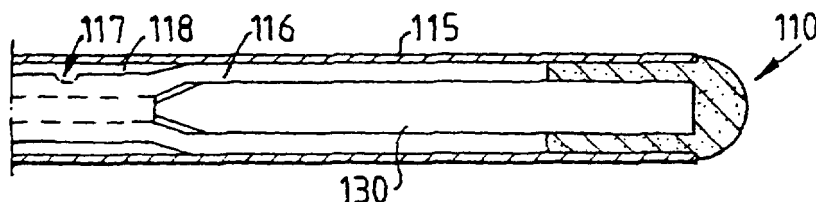
(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
18 January 2001 (18.01.2001)

PCT

(10) International Publication Number
WO 01/03752 A1

- (51) International Patent Classification⁷: **A61M 1/00, 25/095**
- (21) International Application Number: **PCT/SE00/01495**
- (22) International Filing Date: **14 July 2000 (14.07.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
9902695-7 14 July 1999 (14.07.1999) **SE**
- (71) Applicant (*for all designated States except US*): **CMA/MICRODIALYSIS AB [SE/SE]; Box 2, S-171 18 Solna (SE).**
- (72) Inventor; and
- (75) Inventor/Applicant (*for US only*): **JOHANSSON, Roger [SE/SE]; Valloxvägen 14, S-741 42 Knivsta (SE).**
- (74) Agents: **BERG, S., A. et al.; Albihns Patentbyrå Stockholm AB, P.O. Box 5581, S-114 85 Stockholm (SE).**
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— *With international search report.*
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **MICRODIALYSIS PROBE**

(57) Abstract: The invention concerns a microdialysis probe, comprising a dialysis membrane (115, 415) located and supported between a closed distal end of the probe and a proximal end of the same, said membrane (115, 415) essentially surrounding a space (118, 418) for passage of perfusion liquid; said probe having inlet and outlet means (107, 108; 407, 408) for perfusion liquid, characterized by presence of a position indicating object imparting such characteristics to the distal part of the probe as to allow non-invasive examination of the location of the distal part of the microdialysis probe.

1 / 3

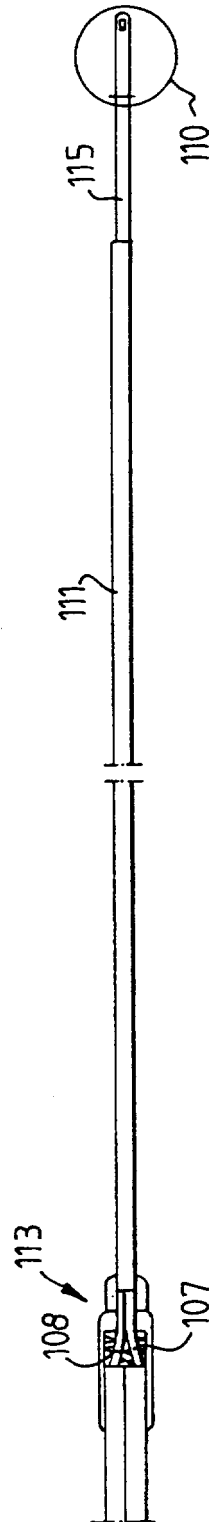


FIG. 1

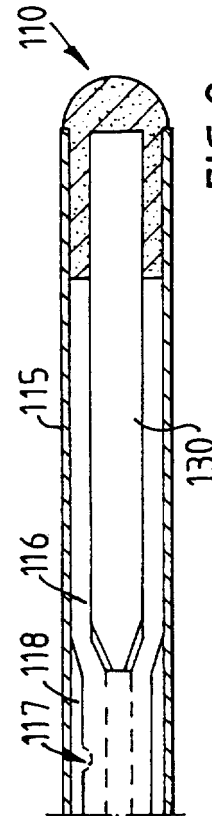


FIG. 2

2 / 3

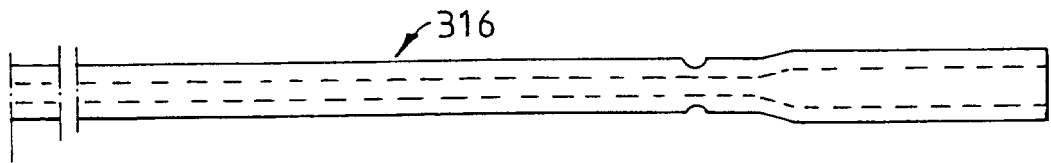


FIG. 3a

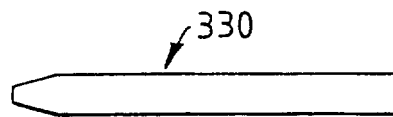


FIG. 3b

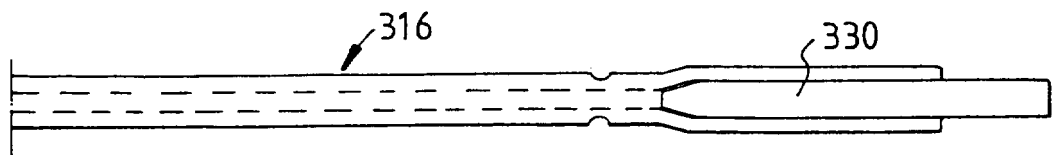
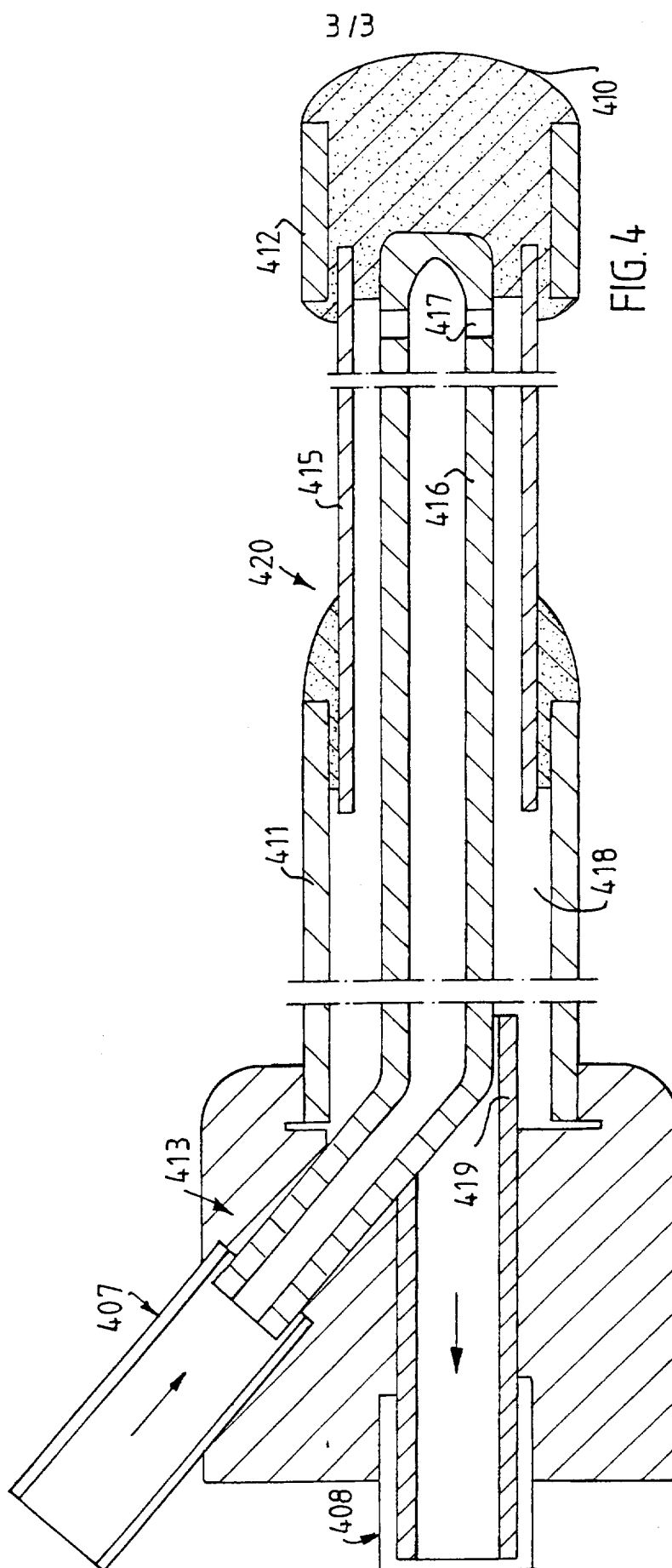


FIG. 3c



COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: MICRODIALYSIS PROBE

the specification of which. (check one)

REGULAR OR DESIGN APPLICATION

- ☐ is attached hereto.
- ☐ was filed on _____ as application Serial No. _____ and was amended on _____ (if applicable).

PCT FILED APPLICATION ENTERING NATIONAL STAGE

- ☒ was described and claimed in International application No. PCT/SE00/01495 filed on July 14, 2000 and as amended on _____ (if any).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

PRIORITY CLAIM

I hereby claim foreign priority benefits under 35 USC 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed.

PRIOR FOREIGN APPLICATION(S)

Country	Application Number	Date of Filing (day, month, year)	Priority Claimed
Sweden	9902695-7	14 July 1999	Yes

I hereby claim the benefit under Title 35, United States Code §119(e) of any United States provisional patent application(s) listed below:

Application No.	Filing Date	Status (patented, pending abandoned)
-----------------	-------------	--------------------------------------

(Complete this part only if this is a continuing application.)

I hereby claim the benefit under 35 USC 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of 35 USC 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

Application No.	Filing Date	Status (patented, pending abandoned)
-----------------	-------------	--------------------------------------

POWER OF ATTORNEY

The undersigned hereby authorizes the U.S. attorney or agent named herein to accept and follow instructions from **ALBIHNS STOCKHOLM** as to any action to be taken in the Patent and Trademark Office regarding this application without direct communication between the U.S. attorney or agent and the undersigned. In the event of a change in the persons from whom instructions may be taken, the U.S. attorney or agent named herein will be so notified by the undersigned.

As a named inventor, I hereby appoint the registered patent attorneys represented by Customer No. 000466 to prosecute this application and transact all business in the Patent and Trademark Office connected therewith, including. **Robert J. PATCH, Reg. No. 17,355, Andrew J. PATCH, Reg. No. 32,925, Robert F. HARGEST, Reg. No. 25,590, Benoît CASTEL, Reg. No. 35,041, Thomas W. PERKINS, Reg. No. 33,027, Roland E. LONG, Jr., Reg. No. 41,949, and Eric JENSEN, Reg. No. 37,855,**

c/o YOUNG & THOMPSON,
Second Floor,
745 South 23rd Street,
Arlington, Virginia 22202.

Address all telephone calls to Young & Thompson at 703/521-2297. Telefax: 703/685-0573.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of sole or first inventor: Roger JOHANSSON

Inventor's signature: [Signature] Date: 07/22/04

Residence: Knivsta, Sweden  Citizenship: Sweden

Post Office Address: Valloxvagen 14, S-741 42 Knivsta, Sweden

Full name of second joint inventor, if any:

Inventor's signature: _____ Date: _____

Residence: _____ Citizenship: _____

Post Office Address:

Full name of third joint inventor, if any:

Inventor's signature: _____ Date: _____

Residence: _____ Citizenship: _____

Post Office Address:

Full name of fourth joint inventor, if any:

Inventor's signature: _____ Date: _____

Residence: _____ Citizenship: _____

Post Office Address: